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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,699	06/14/2002	Ikuo Nishimoto	082376-000000US	2315

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EXAMINER	
LAMBERTSON, DAVID A	

ART UNIT	PAPER NUMBER
1636	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,699	NISHIMOTO, IKUO	
	Examiner	Art Unit	
	David A. Lambertson	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *3 and 9* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8 and 10-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I (Claims 1, 2, 4-8 and 10-13) in the response filed December 2, 2003 is acknowledged. The traversal is on the ground(s) that the restriction does not accurately reflect the special technical feature of the claimed invention. Applicant argues that the special technical feature of the instant invention is the derivation of a molecule from a cell in an area in an organism affected by a disorder that accompanies cell death. Applicant further indicates that, because there is no art of record disclosing Applicant's technical feature, it distinguishes the claim over the prior art. Finally, Applicant asserts that simply because there are other technical features between the restricted inventions, this is insufficient to warrant the restriction of the groups. This is not found persuasive because of the reasons set forth below.

Firstly, Applicant is attempting to establish a different special technical feature than the one set forth by the Office in the restriction requirement. It is important to note that the Office establishes the nature of the special technical feature in the restriction of applications, and that an acceptable and different special technical feature was established for each of the restricted inventions; this is all that is necessary to properly restrict inventions. Second, there is prior art that reads on the elected invention; therefore Applicant's special technical feature is not distinguishable over the prior art (see the rejections under 35 USC 102(b), set forth below). Additionally, unity of invention does not necessarily require prior art in order to establish distinct special technical features, thus it is possible to restrict inventions in the absence of prior art. Finally, the fact that there are different technical features between the restricted inventions is sufficient to

properly restrict inventions if those features are special technical features. In this instance, the identification of a polypeptide versus a gene (i.e., a nucleic acid) requires different procedures, and these procedures represent special technical features because one of skill in the art would recognize that art disclosing a method of detecting a nucleic acid would not be identical to a method of identifying a polypeptide.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13 are pending in the instant application. Claims 3 and 9 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed December 2, 2003.

Claims 1, 2, 4-8 and 10-13 are ready for examination in the instant application, where the claims are being examined with regard to a method of identifying a gene (i.e., a nucleic acid), and an Office Action on the merits is contained below.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). However, it is noted that there is no English translation of either foreign patent document, thus an accurate determination of the priority claim in terms of support for the invention cannot be made regarding those documents. As a result, priority is only granted as far as the filing date of the PCT/JP00/06313 application.

Information Disclosure Statement

The information disclosure statement filed June 21, 2002 has been considered, and a signed an initialed copy of the form PTO-1449 is attached to this Office Action. It is noted, that although references AA, AB, AE and AG were not present in the file at the time of the examination, these references were obtained and entered into the file by the Office. In addition, it is noted that although documents AA, AB and AC are indicated as containing translations, only the Abstracts of these documents are translated. As such, only the Abstracts of these documents have been considered with regard to the examination of the application.

Drawings

The drawings are objected to because Figure contains a sequence for which there is no indication of an identifier in either the figure itself, or in the Brief Description thereof. Corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

Claims 1, 4-7 and 10-13 are objected to because of the following informalities: the claims recite non-elected subject matter, specifically a method for the identification of a polypeptide. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the specification coupled with information known in the art without undue experimentation (*United States v. Telectronics.*, 8 USPQ2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is needed is not based upon a single factor but rather is a conclusion reached by weighing many factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988), and the most relevant factors are indicated below:

Nature of the invention. The nature of the invention is a method of identifying a suppressor gene for a disorder, wherein the gene is derived from a tissue of an organism suffering from a disorder which is accompanied by cell death. The invention requires knowing the disorder that is being suppressed, as well as being able to discern which genes are suppressors of that disorder. The instant claim does not set forth the nature of the disorder that is being analyzed for suppressors, nor does the claim set forth any method steps in which a suppressor gene can be discerned from a non-suppressor gene.

In essence, it would seem from the claimed method that any nucleic acid that is derived from such a tissue is necessarily a suppressor of any disorder.

Scope of the invention. The scope of the invention is very broad, and encompasses the identification of any gene, some of which may be suppressors, but the preponderance of which will have no suppressive effect on any disorder. Furthermore, the scope of the invention is very broad with respect to the disorders for which a suppressor is sought. As it regards these matters, the skilled artisan requires the ability to discern which of the multitudes of genes represent a suppressor relative to those genes that have no suppressive effects, and must do so with respect to the broad range of disorders that are set encompassed by the instant claim language.

Number of working examples and Guidance provided by applicant. The instant specification focuses mainly on the identification of suppressor genes as they relate to neurodegenerative disorders, such as Alzheimer's disease. Although the instant specification describes method steps to be performed when identifying suppressor genes for such neurodegenerative disorders, neither the specification nor instant claim indicates what steps are to be performed with regard to identifying suppressors for just any disorder that accompanies cell death. Specifically, one of skill in the art could not use the invention as claimed because the skilled artisan would be unable to perform the necessary method steps to discern a suppressor from a non-suppressor gene for any particular disorder that is accompanied by cell death. This is particularly difficult because the skilled artisan cannot discern what steps are to be performed for a given disorder, as it would appear that the method steps to identify a suppressor from a non-suppressor would be different depending upon the disorder that is being screened against. As such, given

the instant claim language, the skilled artisan could not use the invention as recited in the claim based on the instant specification, because it is unclear how to discern a suppressor gene from a non-suppressor gene.

Unpredictability of the art and Amount of experimentation required. The invention is highly unpredictable because the skilled artisan cannot fully perform the claimed method with a reasonable expectation of success. This is because the skilled artisan cannot be apprised of what method steps must be performed in order to accurately discern between a suppressor and non-suppressor gene for a given disorder. While a number of genes can be identified from a given tissue or cell type, there is no clear method step by which the skilled artisan can conclude that any particular gene is a suppressor (or a non-suppressor, as the case may be). In the absence of a method step that performs the function of identifying a suppressor (versus a non-suppressor gene) for a given disorder, the skilled artisan cannot know if the method has been performed, and thus cannot use the invention as claimed.

In conclusion, Applicant's claim is directed to the identification of a suppressor gene for a disorder associated with cell death. However, the claim does not contain a step whereby one of skill in the art can ascertain if the identified gene is a suppressor gene or not, therefore the method cannot be used with any expectation of success. Without a reasonable expectation of success, the method is unpredictable, thereby rendering the claim non-enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 4-8 and 10-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 2, 4-8 and 10-13 recite the terminology "nucleic acid derived from." The specification defines the term on page 12, lines 33-36 of the instant specification as including "nucleic acids obtained from organisms and those synthesized from the nucleic acids, nucleic acids comprising those, and amplified products thereof." This is indefinite for two reasons: first, it is unclear what the metes and bounds of the claim are because, while it is clear that the aforementioned are "included" in the definition of "nucleic acids derived from," it is unclear what else is "included" in the definition; second, it is unclear what method steps are required to "derive" the nucleic acid as set forth in the claims, as the term "derived" necessarily implies that some process must be performed to get to the result.

Claims 1, 2, 4-8 and 10-13 recite the terminology "tissue is derived from." Similar to what is set forth above, it is unclear what steps are required to "derive" the tissue from an area of an organism. Additionally, it is unclear what is included or characterized as a tissue that has been derived from an area (i.e., does this include individual cells, extracts, etc.).

The term "the vicinity of the affected area" in claims 1, 2, 4-8 and 10-13 is a relative term which renders the claims indefinite. The term "the vicinity of the affected area" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. For instance, it is not clear how close in proximity the tissue must be to the afflicted area in order for it to be considered within "the vicinity." For example, it is unclear if the stomach would be considered within the vicinity of the large intestine, etc.

Claims 1, 2, 4-8 and 10-13 are rejected for failing to recite a positive process step which recapitulates the preamble of the claimed method. Without such a step, there is no conclusion or endpoint to the claimed method, therefore the metes and bounds of the claims are indefinite. In other words, without such a step, it is unclear if the method has been performed to completion. It would be remedial to recapitulate the purpose of the method set forth in the preamble of the claim at the end of the claim (i.e., insert "thereby identifying a disorder suppressor gene" at the end of the claim).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

With regard to the indefinite terms set forth in the claims, the following interpretations are being made: (1) a "nucleic acid derived from a tissue" is being interpreted as any nucleic acid; (2) a "tissue derived from an area affected by a disorder" is being interpreted as any tissue culture system comprising cells that exhibit the characteristics of a disorder that accompanies cell death.

Claims 1, 2, 4-8 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Giambarella *et al.* (*EMBO J* **16**:4897-4907, 1997; see entire document; henceforth Giambarella).

Familial Alzheimer's disease (FAD) is a neurodegenerative disease of the cranial nervous system. Mutations in the amyloid precursor protein (APP), in particular mutations at V642, have been shown to be causally related to Alzheimer's disease (AD)(see for instance page 4897, right column, top paragraph). In transgenic mice, overexpression of V642 mutants of APP have been shown to lead to senile plaque formation similar to those seen in AD patients (see for example page 4897, right column, first full paragraph). Interestingly, V642 mutants are capable of inducing apoptotic cell death in neuron-like transformants of COS cells, thereby providing a phenotypic link between cell death and the onset of AD (see for example page 4898, left column, first full paragraph). Thus, it is clear that cells expressing V642 mutants exhibit the characteristics of a disorder related to apoptotic cell death. Using such cells, Giambarella teaches that the expression of a nucleic acid encoding for the C-terminus or the β-adrenergic receptor kinase-1 protein (βARK1) has the capacity to suppress the apoptotic effects of the V642 APP mutants (see for example page 4900, paragraph bridging the left and right columns). Therefore Giambarella anticipates each of the claims for the following reasons:

1. Giambarella teaches the suppression of a disorder associated with apoptotic cell death, by expressing a nucleic acid (encoding a gene) that prevents the onset of the apoptosis. This nucleic acid fits the definition of any nucleic acid, which is the broadest reasonable interpretation of the indefinite term "nucleic acid derived from."

2. The culture system that is used anticipates the limitation "a tissue derived from an area affected by the disorder" because the culture system comprises neuron-like cells that express a causative agent of Alzheimer's disease, and therefore exhibits the characteristics of the disorder.

3. Alzheimer's disease represents a disorder of the cranial nervous system, as defined by the specification.

4. In order to have identified βARK1 as a suppressor of the apoptotic effect of V642 APP mutants, apoptosis would have to be induced either during, before or after the expression of the suppressor nucleic acid.

In conclusion, Giambarella teaches every limitation as set forth in the instant claims, and therefore anticipates the claimed invention.

Claims1, 2, 4-8 and 10-13 are rejected under 35 U.S.C. 102(b) as being anticipated by Guo *et al.* (IDS reference AF; see entire document; henceforth Guo).

Mutations in the Presenilin 1 (PS-1) gene account for a number of autosomal dominant forms of Alzheimer's disease (see for example the Abstract, first line). As stated before (see above rejection), apoptosis and Alzheimer's disease have been phenotypically linked. Importantly, expression of PS-1 mutants in PC12 cells results in increased apoptosis (see for example page 3227, right column, second paragraph). Guo teaches that the co-expression of the protein D28k blocks this apoptosis inducing action of PS-1, thereby serving as a suppressor of a disorder associated with cell death. Therefore, Guo anticipates the instantly claimed invention for the following reasons:

1. Guo teaches the suppression of apoptosis induced in cells that express the PS-1 gene, which has been shown to be causally related to AD, following the expression of the D28k encoding nucleic acid. This nucleic acid is within the interpreted definition of the indefinite term "nucleic acid derived from."

2. The culture system used by Guo meets the interpreted definition of the indefinite term "tissue derived form," because the culture system comprises cells that express a mutant PS-1 gene that has been shown to be causally related to AD onset. Therefore the culture system exhibits the characteristics of a disorder that accompanies cell death, which is exemplified by the fact that the expression of the mutant PS-1 in these cells indeed induces apoptosis.

3. Alzheimer's disease represents a disorder of the cranial nervous system, as defined by the specification.

4. In order to have identified D28k as a suppressor of the apoptotic effect of PS-1 mutants, apoptosis would have to be induced either during, before or after the expression of the suppressor nucleic acid.

In conclusion, Guo teaches every limitation as set forth in the instant claims, and therefore anticipates the claimed invention.

Allowable Subject Matter

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Lambertson whose telephone number is (571)

272-0771. The examiner can normally be reached on 6:30am to 4pm, Mon.-Fri., first Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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JAMES KETTER
PRIMARY EXAMINER